

## Reviewer Report

**Title:** The Gene Expression Deconvolution Interactive Tool (GEDIT): Accurate Cell Type Quantification from Gene Expression Data

**Version:** Original Submission    **Date:** 9/16/2020

**Reviewer name:** Paul Pavlidis, Ph.D.

### Reviewer Comments to Author:

For the most part the responses are sufficient and the authors have addressed the concerns, and the manuscript is improved. I especially appreciate that claims have been toned down and better contextualized.

A small issue remains about minor comment 6. My point was that the readers should be made clearly aware that doing three deconvolutions is not ideal, and strictly speaking invalid (e.g. cell contents totalling over 100%). I suggested two hypothetical ways to avoid this and am not at all surprised it's not easy to fix with data on hand. In the context of the demonstration in this particular study, what the authors did originally is acceptable. The problem I raised is if people start copying that practice in their own studies, and in the authors' own interest they presumably wouldn't want to be seen as endorsing it. The statement in the supplement that "creating a comprehensive reference from single cell data will likely produce superior results" should be more prominent, and it's not just about superior results, it's also about validity of having a single reference vs. multiple independent deconvolutions.

To be concrete, I'd suggest that in the main body a parenthetical could be added to the effect that "it would be more appropriate to have a single reference containing all cell types and performing a single deconvolution; see supplement for discussion". As it stands I don't think the addition to the supplement is referenced in the main paper.

## Methods

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